C. REMARKS

The claims have been amended in order to place the application in better form.

Claims 1 - 29 previously have been cancelled with prejudice.

Claims 37 and 43 have been cancelled without prejudice. The fact that Claims 37 and 43 have been cancelled without prejudice is not to be construed as an admission by Applicants or Applicants' attorneys that such claims are unpatentable and Applicants reserve the right to prosecute such claims in a continuing application.

Claims 30, 35, and 38 have been amended. The fact that Claims 30, 35, and 38 have been amended is not to be construed as an admission by Applicants or Applicants' attorneys that such claims, prior to the amendment thereof, were unpatentable.

Claims 30-32 and 35-37 stand rejected under 35 U.S.C.102(b) as being anticipated by Xia, et al. This rejection is respectfully traversed.

The present invention is directed to an antibody which elicits alloantigen specific hyporesponsiveness and which binds to the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB 11423, as defined broadly in Claim 30, and to a cell line which produces such an antibody, as defined in Claim 35.

It is the Examiner's position that Xia teaches LO-CD2a binding specificity and that Xia, as a whole, including Tables 1-6 and Figures 1-4, provide a profile of binding specificities and functional properties in a quantitative and qualitative manner.

In response, Applicants assert that the disclosure in Xia with respect to LO-CD2a provides no information with respect to the epitope to which LO-CD2a binds.

With respect to the rejection under 35 U.S.C. 102(b), the burden is upon the Examiner to show that Xia discloses all of the elements and limitations of Applicants' claimed antibody, i.e., an antibody which elicits alloantigen specific hyporesponsiveness

and which binds to the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB11423. (See Scripps Clinic & Research Foundation v. Genentech, Inc., 927 F.2d 1576, 18 U.S.P.Q.2d 1010 (C.A.F.C. 1991).) All of the elements, necessarily or inherently, must be present. The burden is upon the Examiner to show that by following the teachings of Xia, one must obtain an antibody that necessarily or inherently binds to the same epitope as the deposited antibody. (See Continental Can Co. v. Monsanto, 948 F.2d 1264, at 1268; 20 U.S.P.Q.2d 1746, at 1749.) The mere possibility or even the probability that one could obtain an antibody that binds to the same epitope as the deposited antibody by following the teachings of Xia is insufficient under the patent law to establish anticipation See Continental, 984 F.2d 1264, at 1269, 20 U.S.P.Q.2d, at 1749-1750, which held that:

> Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.

Xia discloses a basic standard procedure for producing monoclonal antibodies. The burden is on the Examiner to show that by following such procedure, one obtains an antibody that necessarily or inherently binds to the same epitope as the deposited antibody.

Xia states that one of the antibodies recovered by the procedure is the LO-CD2a antibody; however, in order to anticipate the Examiner must demonstrate that if the Xia procedure is repeated, one skilled in the art necessarily would be able to obtain the claimed antibody.

Xia discloses a standard procedure that produces CD2 monoclonal antibodies and, as recognized in the art (and as disclosed by Xia), such procedure would produce a myriad of CD2 antibodies.

There is nothing of record that would indicate that because LO-CD2a antibody was produced by Xia by such procedure that it necessarily would be produced again if the procedure were repeated.

In addition, if such an antibody were among the wide variety of antibodies produced by such a procedure, there is no evidence that one skilled in the art necessarily would be able to obtain such antibody from among the wide variety of other possible antibodies that may be produced by following the teachings of Xia.

The Examiner speculates that in repeating the procedure of Xia, an antibody as claimed would be produced and further speculates that the properties disclosed by Xia uniquely identify antibodies of the type claimed so that by testing for such properties, one skilled in the art necessarily would obtain the claimed antibody. Such speculation is not sufficient to meet the burden of proof required to establish that Xia anticipates Claims 30-32 and 35-37.

In contrast to the Examiner's speculation, Applicants previously have submitted evidence that the antibodies of Claims 30-32 and 35-37 would not be obtained necessarily by following the teachings of Xia.

Such evidence has been presented in the Declaration of Dr. Bierer. Dr. Bierer has testified that if one skilled in the art repeated the procedure disclosed by Xia, one skilled in the art would not be able to identify which of the antibodies was LO-CD2a or an antibody which binds to the same epitope as the deposited antibody. (Bierer Declaration, Paragraphs 5 and 6.) Thus, by following the teachings of Xia, one skilled in the art would not obtain necessarily or inherently an antibody which binds to the same epitope as the deposited antibody.

More particularly, all that Xia discloses is that LO-CD2a antibody has characteristics which are common to CD2 antibodies as a class. (See Bierer Declaration, Paragraph 7.) Such characteristics are general characteristics which are possessed by other CD2 antibodies and, therefore, screening antibodies for such characteristics would not indicate whether or not a CD2 antibody were LO-CD2a, or whether or not an antibody is an antibody which binds to the same epitope as the deposited antibody. (Bierer Declaration, Paragraph 8.)

The data presented by Xia do not identify uniquely LO-CD2a or an antibody which binds to the same epitope as the deposited antibody. In order to identify or characterize LO-CD2a uniquely, one skilled in the art would need information with respect to the specific epitope to which LO-CD2a binds, and there is no such information in Xia. (Bierer Declaration, Paragraphs 9 and 10.) Because Xia lacks such information, Xia does not teach that the LO-CD2a antibody necessarily or inherently binds to the same epitope as the deposited antibody.

Although Xia, at Page 320, indicates that LO-CD2a binds to an epitope that is different from the epitope to which antibody D66 binds, Xia does <u>not</u> identify either epitope, and the information provided by Xia would not distinguish LO-CD2a from the plurality of other antibodies. (Bierer Declaration, Paragraph 11.)

The data shown in Table 1 and in Figures 1A and 1B of Xia merely define characteristics with respect to LO-CD2a which are characteristic of CD2 antibodies as a class and do not identify uniquely LO-CD2a or an antibody which binds to the same epitope as the deposited antibody. (Bierer Declaration, Paragraphs 12 and 13.)

Furthermore, the reactivity pattern shown in Figures 1A and 1B indicate that LO-CD2a is not different statistically from a known CD2 antibody OKT11. (Bierer Declaration, Paragraph 14.)

Although Table 4 of Xia indicates that LO-CD2a differs from antibody T11 in that LO-CD2a does not react with CEM cells whereas the known CD2 antibody T11 does react with CEM cells, it is well known in the art that other CD2 antibodies do not react with CEM cells and do react with MOLT4 cells, HPB-ALL cells and Jurkat cells, as does LO-CD2a. Thus, the characteristics of LO-CD2a shown in Table 4 of Xia do not identify LO-CD2a uniquely. (Bierer Declaration, Paragraph 16.)

Tables 2, 3, 5, and 6 of Xia also define characteristics of LO-CD2a; however, like Tables 1 and 4, and Figures 1A and 1B, these tables disclose characteristics of LO-CD2a that do not identify LO-CD2a uniquely. Table 2 discloses the reactivity of LO-CD2a with various leukemia cell types. Table 3 discloses the reactivity of LO-CD2a with various non-T-cell types, such as B-lineage cells and myeloid cell lines. Table 5 discloses the effect of LO-CD2a on rosette formation, and Table 6 discloses the effect of LO-CD2a on lymphocyte proliferation induced by lectins, OKT3 antibody, or antigens. These tables, like Tables 1 and 4, and Figures 1A and 1B, provide no guidance with respect to the epitope to which LO-CD2a binds specifically.

In addition, although the Examiner has relied upon Figures 2 through 4 as part of his basis for rejecting Claims 30-32 and 35-37 as anticipated by Xia, Applicants note that such figures do not provide any information with respect to LO-CD2a. Figure 2 provides data with respect only to LO-CD6a, LO-CD4a, LO-Tmat, OKT11, and B4 antibodies. Figure 3 provides data with respect only to LO-CD4a, LO-CD4b, OKT4, and OKT8 antibodies. Figure 4 provides data with respect to the inhibition of Leu3-a binding

by LO-CD4a and LO-CD4b antibodies, and to the inhibition of T12 binding by LO-CD6a and LO-Tmat antibodies. Such figures provide no information with respect to LO-CD2a.

The characteristics shown in Xia with respect to LO-CD2a are characteristics possessed in general by CD2 antibodies as a class, and some of such characteristics are similar to those of specific known CD2 antibodies. Such characteristics do not characterize LO-CD2a uniquely, and do not define the specific epitope to which LO-CD2a binds. Therefore, one skilled in the art who follows the teachings of Xia would not be able to characterize LO-CD2a uniquely and, therefore, would not necessarily or inherently produce an antibody which binds to the same epitope as the deposited antibody.

Xia merely teaches that LO-CD2a antibody is an antibody that binds to CD2. Although it may be possible that the LO-CD2a antibody of Xia binds to the same epitope as the deposited antibody, such possibility is insufficient to establish anticipation. The burden is upon the Examiner to show that the LO-CD2a antibody of Xia necessarily or inherently binds to the same epitope as the deposited antibody, and in light of the lack of information in Xia that would characterize or identify LO-CD2a uniquely and identify the epitope to which LO-CD2a binds, the Examiner clearly has failed to meet such burden. Therefore, Xia does not teach one skilled in the art, necessarily or inherently, as is required under the patent law for anticipation, to produce the claimed antibody, i.e., an antibody which binds to the same epitope on human lymphocytes as the deposited antibody.

Because Xia discloses only that LO-CD2a antibody has characteristics which are common to CD2 antibodies as a class, those skilled in the art also would recognize that such characteristics do not enable one skilled in the art to identify uniquely LO-CD2a or

an antibody which binds to the same epitope as the deposited antibody. Such characteristics are not suitable for distinguishing LO-CD2a from other antibodies produced by the general procedure disclosed by Xia, or to enable one skilled in the art to identify an antibody which binds to the same epitope as the deposited antibody.

Furthermore, the Examiner has provided no evidence of record which indicates that the LO-CD2a antibody as described by Xia was made available to the public prior to the effective filing date of the above-identified application. Thus, in light of the absence of teachings in Xia establish that one skilled in the art necessarily would obtain the antibodies of Claims 30-32 and 35-37, coupled with the lack of evidence of public availability of LO-CD2a prior to the effective filing date of the above-identified application, Xia clearly does not enable one skilled in the art to obtain necessarily an antibody which binds to the same epitope as the deposited antibody.

Thus, because following the teachings of Xia does not necessarily or inherently enable one to obtain LO-CD2a and other antibodies that bind to the same epitope as opposed to CD2 antibodies in general, Xia does not anticipate an antibody which binds to the same epitope as the deposited antibody. As stated previously, the possibility that the claimed antibody may be produced by following the teachings of Xia is not sufficient to establish anticipation. Because Xia does not enable one skilled in the art to obtain necessarily an antibody which binds to the same epitope as the deposited antibody, Xia cannot and does not anticipate an antibody which binds to the same epitope as the deposited antibody. (See Transclean Corp. v. Bridgewood Services, Inc., 290 F.3d 1364, 62 U.S.P.Q.2d 1865 (C.A.F.C. 2002); Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc., 246 F.3d 1368 (C.A.F.C. 2001), at 1374, 58 U.S.P.Q.2d 1508; Chester v. Miller, 906 F.2d 1574 (C.A.F.C. 1990), at 1577, 15 U.S.P.Q.2d 1333, at

1336; Akzo N.V. v. U.S. International Trade Commission, 808 F.2d 1471 (C.A.F.C. 1986), at 1479, 1 U.S.P.Q.2d 1241, at 1245; Paperless Accounting, Inc. v. Bay Area Rapid Transit System, 804 F.2d 659 (C.A.F.C. 1986), at 665, 231 U.S.P.Q. 649, at 653.)

It is therefore respectfully requested that the rejection under 35 U.S.C. 102(b) be reconsidered and withdrawn.

Claims 30, 31, and 37 stand rejected under 35 U.S.C. 102(b) as being anticipated by Olive, et al., and as further evidenced by Denning, et al. and Xu, et al. This rejection is respectfully traversed.

Olive and Denning disclose an antibody that has been called the "Workshop No. 448" antibody or the "35.1" antibody. Xu discloses that the 35.1 antibody competes with the LO-CD2a antibody BTI-322 in CD2 binding.

As indicated in Xu, however, the 35.1 antibody does not elicit alloantigen specific hyporesponsiveness. At Page 481, column 2, lines 22-29, Xu states that

> "The anti-CD2 antibody BTI-322 is well known for its potent immunosuppressive activity in vitro and effective T cell depletion in vivo. It has distinct characteristics not shared with other anti-CD2 antibodies, namely the generation of unresponsiveness upon restimulation with the same antigen after primary stimulation in the presence of BTI-322. Even the antibody 35.1 (mouse IgG2a-K, ATCC), that competes with BTI-322 in CD2 binding, does not show this effect ... ."

Thus, the 35.1 antibody which is disclosed in Olive, Denning, and Xu dos not elicit alloantigen specific hyporesponsiveness, in contrast to the claimed antibody which does elicit alloantigen specific hyporesponsiveness. Therefore, Olive, Denning, and Xu do not anticipate the claimed antibody, and it is therefore respectfully requested the rejection under 35 U.S.C. 102(b) be reconsidered and withdrawn.

Claims 30-43 stand rejected under 35 U.S.C. 103 as being unpatentable over Xia, et al. in view of Queen, et al. or Newman, et al., and in further view of Guckel, et al., or Bromberg, et al., or Hafler, et al., or Chavin, et al., or Faustman. This rejection is respectfully traversed.

Xia, alone or in view of the other cited references, does not render the claims unpatentable.

One skilled in the art, from reading Xia, would not be enabled to obtain an antibody which binds to the same epitope as the antibody produced by the deposited cell line.

As indicated in the Declaration of Dr. Bierer, the characteristics which are defined in Xia, et al. are not characteristics which define a specific epitope. The characteristics disclosed by Xia are characteristics common to CD2 antibodies as a class. Thus, even if one skilled in the art were able to identify an antibody which had characteristics similar to those of the LO-CD2a antibody disclosed in Xia, et al., such characteristics do not indicate whether or not an antibody binds to the same epitope as the deposited antibody in that such characteristics are those generally possessed by CD2 antibodies.

As indicated in Dr. Bierer's declaration, from the teachings of Xia, one skilled in the art would have no way of knowing which, if any, of the antibodies which would be produced by the general procedure disclosed by Xia, et al. is LO-CD2a or which binds to the same epitope as the antibody of the present invention in that the characteristics disclosed by Xia do not define LO-CD2a uniquely (distinguishing LO-CD2a from CD2 antibodies as a class) or define which antibodies bind to the same epitope as LO-CD2a or deposited antibody.

The claims of the present application are directed to an antibody which binds to the same epitope as the antibody produced by the deposited cell line. In order to negate the patentability of such claims, it is incumbent upon the Patent Office to provide detailed reasons as to why it believes that the characteristics disclosed by Xia uniquely define antibodies which bind to the same epitope as the antibody produced by the deposited cell line, particularly in view of the Declaration of Dr. Bierer, which indicates clearly that the characteristics included in Xia, et al. are characteristics which are known

to be present in CD2 antibodies as a class, and do not define whether or not an antibody binds to a particular epitope. In particular, as noted by Dr. Bierer, different antibodies which bind to different epitopes have the characteristics disclosed by Xia and, therefore, such characteristics are not suitable for identifying an antibody as claimed.

In view of the fact that Xia does not disclose or render obvious to one of ordinary skill in the art the antibody produced by the deposited cell line and further in view of the fact that the characteristics disclosed by Xia are not characteristics which are related to a specific epitope, Xia does not disclose or render obvious to one of ordinary skill in the art an antibody which binds to the same epitope as the antibody produced by the deposited cell line.

Although Xia at Page 320 indicates that the LO-CD2a antibody binds to an epitope which is different from other antibodies referred to on Page 320, Xia does not identify the epitope to which LO-CD2a binds. Because Xia does not define the epitope, Xia does not make LO-CD2a available to one skilled in the art, and one skilled in the art would not have sufficient information to determine whether or not a produced antibody bound to the same epitope as LO-CD2a. The information provided on Page 320 at best permits one skilled in the art to determine that a produced antibody is not D66. Such information does not enable one to determine whether a produced antibody is LO-CD2a, or an antibody other than LO-CD2a.

The secondary references, i.e., Queen, Newman, Guckel, Bromberg, Hafler, Chavin, and Faustman, add nothing to the disclosure of Xia in that none of these references discloses or even remotely suggests to one of ordinary skill in the art an

antibody which binds to the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB 11423.

Therefore, for the above reasons and others, the cited references do not render Applicants' claimed antibody obvious to one of ordinary skill in the art, and it is therefore respectfully requested that the rejection under 35 U.S.C. 103 be reconsidered and withdrawn.

Claims 30-43 stand rejected under 35 U.S.C. 103 as being unpatentable over Olive, et al., in view of Denning, et al., in view of Queen, et al., or Newman, et al., and further in view of Guckel, et al., or Bromberg, et al., or Hafler, et al., or Faustman. This rejection is respectfully traversed.

As noted hereinabove, Olive and Denning disclose an antibody which does not elicit alloantigen hyporesponsiveness.

Thus, the cited references alone or in combination do not even remotely suggest to one of ordinary skill in the art an antibody which does not elicit alloantigen hyporesponsiveness and which binds to the same epitope as the antibody produced by the cell line deposited as ATCC HB 11423. Therefore, the cited references, alone or in combination, do not render the claimed antibody obvious to one of ordinary skill in the art, and it is therefore respectfully requested that the rejection under 35 U.S.C. 103 be reconsidered and withdrawn.

With respect to the obviousness-type double patenting rejection over Claims 1-4 of U.S. Patent No. 5,951,983, the Examiner is advised that a terminal disclaimer with respect to the '983 patent was filed on February 20, 2004. It is therefore respectfully requested that the obviousness-type double patenting rejection be reconsidered and withdrawn.

For the above reasons and others, this application is in condition for allowance, it is therefore respectfully requested that the rejections be reconsidered and withdrawn and a favorable action is hereby solicited.

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